To: Dourson, Michael[dourson.michael@epa.gov]; Beck, Nancy[Beck.Nancy@epa.gov]; Yamada, Richard (Yujiro)[yamada.richard@epa.gov]; Rodan, Bruce[rodan.bruce@epa.gov]; Bahadori, Tina[Bahadori.Tina@epa.gov]; Morris, Jeff[Morris.Jeff@epa.gov]; Henry, Tala[Henry.Tala@epa.gov]; Orme-Zavaleta, Jennifer[Orme-Zavaleta.Jennifer@epa.gov]; Hanley, Mary[Hanley.Mary@epa.gov]; Bertrand, Charlotte[Bertrand.Charlotte@epa.gov]; Scheifele, Hans[Scheifele.Hans@epa.gov]; Lavoie, Emma[Lavoie.Emma@epa.gov]; Camacho, Iris[Camacho.Iris@epa.gov]; Bateson, Thomas[Bateson.Thomas@epa.gov]; Kraft, Andrew[Kraft.Andrew@epa.gov]
From: Thayer, Kris
Sent: Wed 12/20/2017 2:16:56 PM
Subject: RE: Systematic Review and Risk Assessment

Thanks Michael,

For IRIS implementing SR is a key pillar of conducting credible weight of evidence for HI and identification of studies suitable for dose response. As you indicate, we (as an Agency) are still getting our bearings on understanding of the SR methods and applicability to different Offices with different responsibilities and time/resource pressures.

This is why I'm concerned with identifying harmonization of SR protocols as a short-term goal (in first months of 2018?). I'm honestly not sure it's feasible given the timelines that need to be met. Especially if we want the engagement to be approached with iterations of thoughtful discussion, case examples, public input, and revision.

It would be good to think of messaging around why different SR practices are being implemented in the same agency. This is the case at NTP, CDC, WHO, and EFSA as well as EPA. In fact, I'm not aware of an entity that has a diverse assessment portfolio and has found a way to have one single SR method. It remains an elusive goal. But, I think it's an honest statement that both IRIS and TSCA are starting off with transparent approaches tailored to their workflows, assessment needs, and timelines. And through our SR communities of practice we will look for opportunities to further harmonize and tweak approaches as we gain on the ground experience.

From this perspective, we may even be able to tout the NAS workshop and the public comment period on TSCA documents as an opportunity to get broad feedback on methods for implementing SR. Both of us will learn from the comments received by the other.

My two cents,

Kris

From: Dourson, Michael
Sent: Wednesday, December 20, 2017 8:45 AM
To: Thayer, Kris <thayer.kris@epa.gov>; Beck, Nancy <Beck.Nancy@epa.gov>; Yamada, Richard (Yujiro) <yamada.richard@epa.gov>; Rodan, Bruce <rodan.bruce@epa.gov>; Bahadori, Tina <Bahadori.Tina@epa.gov>; Morris, Jeff <Morris.Jeff@epa.gov>; Henry, Tala <Henry.Tala@epa.gov>; Orme-Zavaleta, Jennifer <Orme-Zavaleta.Jennifer@epa.gov>; Hanley, Mary <Hanley.Mary@epa.gov>; Bertrand, Charlotte <Bertrand.Charlotte@epa.gov>; Scheifele, Hans <Scheifele.Hans@epa.gov>; Lavoie, Emma <Lavoie.Emma@epa.gov>; Camacho, Iris <Camacho.Iris@epa.gov>; Bateson, Thomas <Bateson.Thomas@epa.gov>; Kraft, Andrew <Kraft.Andrew@epa.gov>
Subject: Systematic Review and Risk Assessment

Kris and Colleagues

I very much appreciate the meeting yesterday. It was good to get a better sense of systematic review (SR), and from different perspectives. One way that I am now using to sort through the various schemes is to consider each one of them a method to train younger staff to be good (risk assessment) scientists. Because different offices have different (risk assessment) goals (e.g., NCEA with a focus on hazard identification and dose response assessment; OCSPP with a focus on exposure scenario, point of departure and margin of exposure), it does not surprise me that differences in SR exist.

However, SR is not risk assessment. Part of the problem with IRIS is that while staff training is essential and thus SR is important, getting credible HI and DRA assessments done is expected. The opposite problem occurs in other offices, such as OCSPP, which focus on getting assessments done because of crazy deadlines and insufficient resources, with less emphasis on training staff in the newer risk assessment methods that could increase efficiency. Balance in both assessment and training are needed, and of course, not all EPA offices need to have this same balance.

Scoring studies in SR might not be needed for training folks. From a 38 year risk assessment perspective, however, scoring studies for their usefulness in risk assessment is very helpful.

Cheers!

Michael…

… L. Dourson, PhD., DABT, FATS, FSRA

Senior Advisor to the Administrator

U.S. Environmental Protection Agency

dourson.michael@epa.gov

202-564-2463

www.epa.gov

From: Thayer, Kris
Sent: Wednesday, December 20, 2017 3:36 AM
To: Beck, Nancy <Beck.Nancy@epa.gov>; Yamada, Richard (Yujiro) <yamada.richard@epa.gov>; Rodan, Bruce <rodan.bruce@epa.gov>; Bahadori, Tina <Bahadori.Tina@epa.gov>; Dourson, Michael <dourson.michael@epa.gov>; Morris, Jeff <Morris.Jeff@epa.gov>; Henry, Tala <Henry.Tala@epa.gov>; Orme-Zavaleta, Jennifer <Orme-Zavaleta.Jennifer@epa.gov>; Hanley, Mary <Hanley.Mary@epa.gov>; Bertrand, Charlotte <Bertrand.Charlotte@epa.gov>; Scheifele, Hans <Scheifele.Hans@epa.gov>; Lavoie, Emma <Lavoie.Emma@epa.gov>; Camacho, Iris <Camacho.Iris@epa.gov>; Bateson, Thomas <Bateson.Thomas@epa.gov>; Kraft, Andrew <Kraft.Andrew@epa.gov>
Subject: Background information on study scoring in systematic review

Thanks again for the meeting today. Hopefully both of our programs will benefit from the robust discussion.

As noted today, I am headed out of the country so will unlikely be able to make another meeting this week. However, I wanted to quickly share some of the systematic review guidance materials that we referenced as not supportive of the type of scoring approach we understand is being developed for TSCA.

2011 Institute of Medicine report (where the TSCA definition of systematic review is taken from) https://www.nap.edu/read/13059/chapter/5#132

p. 132 In recent years, systematic review teams have moved away from scoring systems to assess the quality of individual studies towards a focus on the components of quality and risk of bias (Juni, 1999). Quality scoring systems have not been validated. Studies assessed as excellent quality using one scoring method may be subsequently assessed as lower quality using another scoring method (Moher et al., 1996). Moreover, with an emphasis on risk of bias, the SR more appropriately assesses the quality of study design and conduct rather than the quality of reporting.

Cochrane Handbook (the most recognized source of systematic review guidance)
http://handbook-5-1.cochrane.org/chapter_8/8_3_3_quality_scales_and_cochrane_reviews.htm

8.3.3 Quality scales and Cochrane reviews

The use of scales for assessing quality or risk of bias is explicitly discouraged in Cochrane reviews. While the approach offers appealing simplicity, it is not supported by empirical evidence (Emerson 1990, Schulz 1995b). Calculating a summary score inevitably involves assigning 'weights' to different items in the scale, and it is difficult to justify the weights assigned. Furthermore, scales have been shown to be unreliable assessments of validity (Jüni 1999) and they are less likely to be transparent to users of the review. It is preferable to use simple approaches for assessing validity that can be fully reported (i.e. how each trial was rated on each criterion).

The underlying limitations to scoring are considered applicable to a wide variety of evidence

(clinical trials, observational epidemiological studies, animal bioassays, etc.) and whether the assessment is narrative or a meta-analysis. The NCEA comments on the TSCA approach collected and shared by Emma make the same points as outlined in the IOM and Cochrane documents. Thus, we have a convergence of opinions among practitioners of systematic review within NCEA and best practice recommendations from the other fields. In contrast, I am not aware of any current systematic review guidance that recommends the use of numerical scoring. At best, scoring approaches are tolerated when other tools do not exist to evaluate the evidence (e.g., in vitro evidence). However, this is not the case for epidemiological and experimental animal evidence.

If we could resolve the scoring issue, then it would be MUCH easier to have approaches that are consistent.

As an aside, the approach to evaluating epidemiology studies within IRIS is based on the methods outlines in this publication "***ROBINS-I: a tool for assessing risk of bias in non-randomized studies of interventions***", which has been cited almost 175 times since being published in BMJ in 2016. A couple of the IRIS epidemiologists are collaborating with this group to develop a version of this tool targeted to assessing environmental and occupational exposures. This is one strategy we are taking to ensure that the SR methods implemented in IRIS are in sync with the best practices in the broader SR community.

Happy holidays! -k

Kristina Thayer, Ph.D.

Director, Integrated Risk Information System (IRIS) Division

National Center for Environmental Assessment, NCEA

ORD, USEPA

Mail Code: B243-01

Building: Bldg B (Room B211I)

Research Triangle Park, NC 27711

(919) 541-0152 RTP

(202) 564-1771 Ronald Reagan Building (room 51203)

Skype: kristina.thayer

thayer.kris@epa.gov